REMARKS

The Pending Claims

The pending claims are directed to a semiconductor particle complex comprising a semiconductor nanocrystal bound to a cationic polymer capable of enhancing the transport of the semiconductor nanocrystal across a biological membrane. Claims 1, 3-16 and 38-41 are pending and under active consideration. Claims 17-37 are withdrawn and claim 2 is canceled.

The Office Action

Claims 1, 3-16 and 38-41 are rejected.

Claims 1, 3-7, 10-13, 16, 38, 39 and 41 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Rothbard et al. (U.S. Patent No. 6,306,993)

Claims 8, 9, 14, 15, and 40 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Frankel et al. (U.S. Patent No. 5,652,122).

Amendments

No claims are currently amended.

RESPONSE TO THE REJECTIONS

I. Claims 1, 3-7, 10-13, 16, 38, 39 and 41 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Rothbard et al. (U.S. Patent No. 6,306,993). Applicants respectfully traverse this rejection.

The present claims are directed to a semiconductor particle complex comprising a semiconductor nanocrystal bound to a cationic polymer capable of enhancing the transport of the semiconductor nanocrystal across a biological membrane.

According to the Office Action, "since Bawendi and Rothbard both teach using a label such as nanocrystals for cells or cell membrane, it would have been obvious to one of ordinary skills in the art to associate the polymer, which comprises of 6 to 25 Arg residue, taught by Rothbard to the nanocrystals as a fluorescent label and use in the composition of Bawendi because macromolecules such as peptides and oligonucleotides experience difficulty in passing across the biological membrane and having a polymer as that of Rothbard enhances trans-membrane transport." Applicants respectfully disagree.

Provided herewith is a declaration by Joseph Treadway, Ph.D. ("the Treadway Declaration"), describing the particular issues encountered when attempting to transport a semiconductor nanocrystal across a biological membrane. According to the Treadway Declaration, "properties such as solubility, high rigidity, core hydrophobicity, large particle diameter and ionic density adversely affect the nanocrystal's ability to associate with subtituent groups and traverse biological membranes." This is contrasted with the "macromolecules" described in Rothbard, which include peptides and oligonucleotides that purportedly experience difficulty in passing across biological membranes. Peptides, oligonucleotides and the like are themselves biological molecules. They inherently posses properties suited for biological systems. These properties include hydrophilicity, flexiblibity, and limited ionic charges (as compared with nanocrystals). While the "macromolecules" described in Rothbard are generally not free as they please to migrate back and forth across biological membranes, they are relatively unencumbered in membrane transport as compared with semiconductor nanocrystals.

A point made in the Office Action is that precisely because of the unique properties and seemingly difficult transportability issues associated with nanocrystals, one would be motivated to try binding the polyargine moieties taught in Rothbard to the nanocrystals to improve their transportability. This is despite the fact that the macromolecules in Rothbard are hydrophilic and Rothbard warns that "attaching a large hydrophobic moiety may significantly impede or prevent cross-membrane transport due

to adhesion of the hydrophobic moiety to the lipid bilayer." Column 8, lines 15-20. Rothbard goes on to state that "the present invention includes conjugates that do not contain large hydrophobic moieties..." Semiconductor nanocrystals contain hydrophobic moieties. Accordingly, Applicants submit that not only does Rothbard fail to teach, motivate, or provide a reasonable expectation of success in combining the nanocrystals of Bawendi with the polymers in Rothbard for transport across a biological membrane, it actually teaches away from it.

As described in the Treadway Declaration, "Rothbard et al. describes the conjugation of drugs such as paclitaxel (Example 9) and proteins such as ovalalbumin (Example 12) to polymers containing multiple arginine units. Rothbard et al. does not teach how to functionalize any and all macromolecules for transport across biological membranes." As evidenced by aforementioned statements in Rothbard, particle properties such as hydrophobicity can be expected to significantly impede cross-membrane transport. Only after the experiments performed by the Applicants did it become evident that cationic polymers can in fact facilitate cross-membrane transport of semiconductor nanocrystals.

"Slight reflection suggests, we think, that there is usually an element of "obviousness to try" in any research endeavor, that it is not undertaken with complete blindness but rather with some semblance of a chance of success, and that patentability determinations based on that as the test would not only be contrary to statute but result in a marked deterioration of the entire patent system as an incentive to invest in those efforts and attempts which go by the name of "research." In re Tomlinson, 363 F.2d 928, 931 (CCPA 1966).

There simply is no motivation or reasonable expectation of success provided by the combination of Bawendi and Rothbard to infer that a cationic polymer bound to a semiconductor nanocrystal would improve transportability of the nanocrystal. Furthermore, Rothbard in fact teaches away from the use of nanocrystals, for cross-membrane transport. Accordingly, Applicants respectfully submit that the rejections over Bawendi in view of Rothbard under 35 U.S.C.§103(a) are improper and should be withdrawn.

II. Claims 8, 9, 14, 15, and 40 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (US 6,306,610) in view of Frankel et al. (US 5,652,122). Applicants respectfully traverse this rejection.

Claims 8, 9, 14, 15, and 40 are directed to a semiconductor particle complex comprising a semiconductor nanocrystal bound to an HIV tat peptide capable of enhancing the transport of the semiconductor nanocrystal across a biological membrane.

According to the present Office Action, "it would have been obvious to one of ordinary skills in the art to use the HIV tat peptide for transporting biological molecules across the cell membrane as taught by Frankel and attach it to a fluorescence semiconductor nanocrystal which associates to a cell membrane so that when biological molecules to be transported reach the cell membrane, they can be transported effectively and efficiently with the aid of the tat peptide and their activity or measurement can be detected by the nanocrystals since the nanocrystals have a spectral emission that is tunable to a desired wavelength, and wherein said wavelength provides information about a biological state or event." Applicants respectfully disagree.

Similar to Rothbard, the "cargo" molecules in Frankel are also biological molecules (i.e. peptides, nucleic acids, oligosaccharides). They inherently posses properties suited for biological systems, including hydrophilicity, flexiblibity, facile conjugation and limited ionic charges (as compared with nanocrystals). In the numerous examples described by Frankel, each of the "cargo" molecules invariably has these biological properties, with the possible exception of PKAI (protein kinase inhibitor), described in columns 33-35 of Frankel. Although PKAI is a relatively small biological molecule (composed of 20 amino acid residues), it does not have a convenient site for tat conjugation (such as a lysine or cysteine residue) and has shown some solubility/precipitation issues. Interestingly, PKAI is one of the only "cargo" molecules in Frankel not shown to be effectively transported across the biological membrane. Furthermore, where solubility issues arose (column 35, lines 22-25), no results were described/obtained, likely due to the uncooperative nature of the complex.

Accordingly, it is only the cooperative (i.e. soluble and easily binding) molecules that were in fact shown to be effective "cargo" molecules. Based on the foregoing and enclosed declaration, Applicants have made it overwhelming clear that the semiconductor nanocrystals of the present invention simply do not conform to procedures described for transport of peptides, nucleic acids, oligosaccharides and the like. It is <u>despite</u> the teachings of Rothbard and Frankel that Applicants performed the experiments to arrive at the present invention showing enhanced delivery of nanocrystals through association with cationic polymers, <u>not because of them</u>.

CONCLUSION

In view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent at (541) 335-0165.

Respectfully submitted,

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